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Chapter 6
Neuroprosthetics
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- Chapter Objectives

Following this chapter the reader will be able to:

1. Understand the basic principles of operation of neuroprostheses (NPs).
2. Appreciate the historical development of NPs.
3. Assess the main benefits and limitations of existing NPs.
4. Recommend the type of NP that might benefit a particular person.
5. Evaluate new NP technologies as they evolve.

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I. INTRODUCTION

A. Definition.

Neuroprostheses (NPs) are electronic devices that stimulate nerves to improve bodily functions lost as a result of damage to the peripheral or central nervous system. This approach is also called functional electrical stimulation (FES) or functional neuromuscular stimulation (FNS). NPs include both surface stimulators that deliver current through the skin to target nerves and implanted stimulators that deliver current directly to the target nerves. On this definition, NPs range from simple “muscle” stimulators used to increase muscle bulk, to complex devices implanted in the spinal cord and brain. The aim of this chapter is to describe the numerous types of NPs that have been developed since the early days of therapeutic electrical stimulation (TES), with a particular emphasis on those NPs that are useful in functional restoration after spinal cord injury (SCI). The spectacular advances that have occurred in the neurosciences and in biomedical engineering in the last two decades have led to numerous technical advances and innovations. Surface and implanted NPs are now available to assist with a wide variety of functions including hand function, postural control, standing, walking, respiration, micturition and pain control. This chapter will address issues related to the benefits and limitations of these devices and factors affecting the choice of an NP for a particular individual.

B. History.

Electrostatic machines capable of generating single high-voltage pulses were invented in the 1740s. Clinicians very soon began using them to apply single stimuli through pairs of surface electrodes, more to impress than to provide therapy^{1,2}. Michael Faraday’s invention of the induction coil in the mid-19th century allowed continuous trains of stimuli to be delivered to nerves and muscles. “Faradic” stimulation quickly became an important means of experimentally stimulating the brain, spinal cord and peripheral nerves (see Mechanisms below).

Advanced Concept Call-out

The amount of current required to activate muscle fibers is more than 10 times greater than that required to activate the nerve that innervates them, so *muscle* stimulators are really *nerve* stimulators. Denervated muscles cannot be activated with the pulse amplitudes normally used in FES, so individuals with lesions that have destroyed the relevant motoneuron pools in the gray matter of the spinal cord, or the motoneuronal axons in spinal nerves (as occurs in cauda equina lesions), unfortunately often do not benefit from FES.

The first detailed manual of motor points, i.e. locations at which Faradic stimulation through the skin activated muscles at the lowest thresholds, was published in 1867³.

Electrical stimulation continued to be used at the fringes of medicine until the 1960s, when the advent of the transistor allowed stimulators to become portable enough to be used in activities of daily life (ADL).

II. MECHANISMS

A. Electrical stimulation of nerves.

Faradic stimulation consists of delivering trains of very brief pulses of electrical current through pairs of electrodes applied to bodily tissues. Electrodes applied to the skin surface are made of a conductive material, e.g. metal or carbonized rubber often with a soft conductive material such as a

moistened cloth pad or a gel coating, that forms an intimate and even contact with the skin surface and thereby avoids hot-spots of high current density. Implanted electrodes are insulated leads with small conductive terminals made of a biologically compatible metal such as stainless steel or platinum-iridium. The terminals are usually built into a non-conductive substrate such as a silastic button (epimysial electrodes), a silastic nerve cuff or an insulated cannula (brain or epidural spinal cord stimulation).

Each pulse of current lasts from 50 to 300 microseconds. Surface stimulation requires currents ranging from 10 to 100 mA and voltages ranging from 10 to 100V, depending on the electrode surface area. Implanted electrodes can activate the nerves they contact with currents in the range 0.1 to 2 mA and voltages in the range 0.1 to 2 volt between the electrode terminals. This is because implanted electrodes allow the current to be delivered directly to the nerve rather than being dispersed through a large volume of tissue.

A single pulse delivered to a motor nerve causes the muscle to twitch once. Repeated pulses cause repeated twitches. Each twitch lasts about $1/20^{\text{th}}$ of a second so when pulses are repeated at a rate greater than 20/s the twitches fuse and the muscle contracts smoothly (this is called a tetanic contraction or tetany). More force can be produced at higher rates, but the increase levels off at around 35 to 45 pulses/second. Fatigue sets in more rapidly the faster the pulse rate. A good compromise between force and fatigue is usually reached between 30 and 40 pulses/second.

The relationship between voltage, current and resistance

Voltage is the product of current and resistance ($V = IR$). To understand current and voltage, think of water being pushed through a shower head. The flow of water per second is equivalent to current I . The pressure drop from inside to outside the shower head is equivalent to voltage V . The smaller the holes in the shower head, the greater the resistance to flow R and so the smaller the current. You can force the same amount of water through smaller holes by increasing the pressure inside the shower head. So flow (current) clearly depends on both the pressure drop (voltage) and resistance.

NP stimulators have electronic circuitry that controls either the voltage or current using feedback. If the current is feedback-controlled, the voltage is automatically adjusted on a moment-to-moment basis so that the same current is delivered, regardless of the impedance presented by the electrodes and tissue. The result is that if the electrode contact is poor (analogy: smaller holes in the shower head), impedance is high and so the stimulator automatically increases the voltage to maintain current flow through the smaller contact area. This ensures a constant level of activation of the target nerves but it can cause skin burns. On the other hand if voltage is feedback-controlled and electrode contact is poor, the amount of current pushed through is less and the nerve may not be adequately stimulated, but there is little risk of skin burns.

The advantage of current-controlled stimulators is that the device always attempts to deliver the same current regardless of the impedance, thereby ensuring stimulation, but with the risk of local tissue damage. Voltage-controlled stimulators always try to deliver the desired voltage. Therefore that if the electrodes make poor contact, less current will flow. There is no risk of damage to the tissue, but the nerve may not be activated. Often in less sophisticated stimulators, neither voltage nor current are feedback-controlled. On the other hand, in advanced current-controlled stimulators,

impedance is monitored and current is limited when the impedance is high, which is the best of both worlds.

B. Therapeutic carry-over effects

Electrical stimulation of muscles has long been known to have carry-over or therapeutic effects⁴⁻⁶, especially in conjunction with voluntary exercise training⁷⁻¹⁰. Surface stimulators triggered during attempted functional tasks (Fig. 1A) or by voluntary EMG activity (Fig. 1B¹¹) have been used in some clinics for FES-assisted motor retraining of the upper extremity^{9,12}. The mechanism of carry-over is poorly understood. Short-term carry-over lasting less than a few hours may result from short-term changes in the energetics of neuromuscular activation whereas long-term carry-over lasting weeks or months is usually attributed to muscle strengthening, neural plasticity or both¹³⁻¹⁵.

III. TYPES OF NEUROPROSTHESES

A. Surface FES devices.

1. Surface stimulation devices for enhancing walking function.

The first portable functional electrical stimulation (FES) device was a surface stimulator that delivered trains of stimuli to the common peroneal nerve to correct footdrop in hemiparetic people (Liberson *et al.*, 1961). This invention was further developed and commercialized in Europe in the 1960s by a group in Ljubljana led by Lojze Vodovnik (the FEPO: functional electrical peroneal orthosis¹⁶). Since then, portable footdrop stimulators of various designs have been used by well over 10,000 people world-wide. Most users have been individuals with stroke, though some individuals with SCI have successfully used them too. Standard physical therapy stimulators equipped with underheel sensors to trigger stimulation (and hence muscle activation) appropriately timed to the gait cycle have also been used as footdrop stimulators in clinics for many years (e.g. the original Medtronic Respond® unit, and currently the Empi 300PV®). By the year 2000 there had been three successful initiatives in countries with public health care systems to provide footdrop stimulators to hemiparetic people on a routine basis: Yugoslavia¹⁷, Denmark (Dr. Benny Klemar, personal communication) and the UK¹⁸. In the USA, a ruling by the Centers of Medicare and Medicaid Services (CMS) in the 1980s precluded reimbursement of neuromuscular stimulators prescribed for neurological disorders (although paradoxically, reimbursement is available when the same devices are used for treating back pain, which generally involves the neuromuscular system). Consequently, adoption of footdrop stimulators in the USA has been slow and patchy. Currently the three main footdrop stimulators available in North America on a self-pay basis are the Odstock®¹⁹, the WalkAide® (Fig. 1F²⁰) and the Bioness L300® (Fig. 1G, <http://bioness.com/products/l300.htm>). They are proving popular and effective, so pressure may grow on CMS to provide them with a reimbursement code. They can be effective in individuals with SCI whose main locomotor problem is footdrop.

The Parastep®, a multi-electrode bilateral FES stimulator used in conjunction with a walker and controlled by hand-switches, was introduced commercially in the 1980s. Up to six muscles were stimulated, three in each leg (foot dorsiflexors, quadriceps and gluteus medius). The device is primarily used by individuals who have complete paraplegia. These individuals have the arm and hand function required to control the device, and they lack sensation in the legs that would preclude the use of high levels of stimulation. Users must have intact lower motor neuron function in the

legs (see the chapter Overview of Spinal Cord Injury). Studies have shown that although ambulation was enabled or improved by this system, the metabolic costs were generally high²¹⁻²³. A study in France came to the following conclusion: “In spite of its ease of operation and good cosmetic acceptance, the Parastep approach has very limited applications for mobility in daily life, because of its modest performance associated with high metabolic cost and cardiovascular strain. However, it can be proposed as a resource to keep physical and psychological fitness in patients with SCI”²⁴.

In the last few years surface FES has been combined with treadmill training and body weight support for locomotor training. In the first study of its kind on nineteen individuals with chronic incomplete SCI (ASIA C), overground and treadmill gait speed more than doubled after 3 months of 1.5 hours, 3 days/week FES + partial weight support training²⁵. The overall conclusion on surface FES for gait after SCI reached in the SCIRE metastudy²⁶ was that “FES-assisted walking can enable walking or enhance walking speed in incomplete SCI or complete (T4-T11) SCI. Regular use of FES in gait training or activities of daily living can lead to improvement in walking even when the stimulator is not in use”.

2. Surface stimulation devices for enhancing hand function.

As with many early FES studies the first experiments exploring FES for upper extremity function were performed by Vodovnik and colleagues in Ljubljana, Slovenia^{27, 28}. In the late 1970s a group at Rancho Los Amigos in Los Angeles, USA developed a therapeutic program for hand function within their clinic, which involved dozens of individuals performing daily FES-assisted biofeedback exercises²⁹. In the 1990s, two designs of surface stimulator for hand function were developed for people with C6-C7 quadriplegia, the Handmaster® (Fig 1D^{30, 31}) and the Bionic Glove® (Fig. 1E^{32, 33}). A clinic-based device, the ETHZ Paracare®, was developed in Switzerland and has undergone two pilot studies^{34, 35}.

The Handmaster®, manufactured by Ness Ltd. in Israel, was medically reimbursed in Holland for several years as a functional splint. Recently it has been sold to clinics and private users in the US under the proprietary name Bioness H200®. It comprises a hinged wrist-forearm splint with a stimulator box electrically connected to the splint via a cable. Electrodes deployed on detachable panels inside the splint deliver trains of stimuli to combinations of three or four motor points. Stimulation is controlled by a push-button on the stimulator or a switch on the part of the orthosis overlying the medial heel of the hand. A recent study in eight individuals with C5-6 SCI reported significant improvements in hand function after 3 weeks of daily usage of the Handmaster®³⁶. Its size and rigid structure makes it suitable mainly for use in the clinic as a therapeutic, rather than as an orthotic device.

The Bionic Glove® comprises a fingerless flexible garment with an in-built stimulator and electrode contacts. The device is controlled by wrist position (flexion and extension) to augment tenodesis grasp and release. In a pilot study on nine individuals with C6-7 SCI using the Bionic Glove® as part of their usual ADLs, grasp force increased 4-fold and performance of manual tasks improved significantly during stimulation³³. In an independent study in twelve individuals with C5-7 SCI, after 6 months of using the Bionic Glove®, voluntary hand function in the absence of the device had improved³⁷. Individuals with C6-7 SCI benefited the most, however higher functioning individuals were less likely to use the device in ADL because the glove required about 5 minutes to don. Further, even though the Bionic Glove® was more form-fitting and compliant than the Handmaster®, it was still considered too bulky to wear during daily life by some individuals.

Various other technical problems were encountered during this 6-month study that led to the overall conclusion that much like the Handmaster®, the Bionic Glove® was more useful as a therapeutic/training device than as a permanent orthosis.

A new, more form-fitting version of the Bionic Glove® is currently being used in a trial involving in-home tele-supervised hand exercise therapy in chronic SCI participants in Edmonton, Canada. The device has a smaller inbuilt stimulator approximately the size of an iPod Nano®, which is triggered by a wireless transmitter worn behind the ear like a hearing aid. The device detects small voluntary toothclicks, allowing the user to activate hand opening and grasp independently of wrist position and without involving the other hand³⁸. Another improvement is that rather than requiring self-adhesive electrodes to be attached to the skin first to make contact with metal-mesh panels inside the glove, low-tack gel electrodes are now attached to the inside of the garment. With this new configuration the system can be donned within approximately 30 seconds. A commercial version will be available to clinical researchers in early 2008. This device has been designed to be used as an orthosis in ADLs as well as for therapeutic training.

Multi-channel upper extremity FES has been tested experimentally in individuals with C3-7 SCI¹⁰. A programmable multi-channel stimulator was used to activate muscles in a sequence that allowed reach and grasp. One of the problems with surface stimulation of large muscles such as biceps and triceps brachii is that during activity the motor points of these muscles can move several centimeters under the skin. This changes the relationship between the stimulating electrode and the motor nerve, thereby changing the amount of muscle activation as the elbow flexes and extends. This in turn results in problems of control. Nonetheless, encouraging therapeutic results were reported in this study.

Arguably, transcutaneous electrical nerve stimulators (TENS) are NPs too. The mechanism of TENS analgesia is thought to be inhibition of nociceptive transmission in the spinal dorsal horn by the activation of large sensory axons (the gate theory of pain:³⁹). One popular version of electrical stimulation for pain relief is interferential stimulation⁴⁰. The mechanism of interferential stimulation is to set up a rotating electric field that activates large afferents deep within bodily tissues by delivering alternating current through several pairs of electrodes and cyclically varying the currents through each pair independently. This approach is also known as “current steering” or “field steering,” when used in implanted dorsal column and cochlear stimulators^{41, 42}. Interferential devices are usually large, expensive and therefore confined to clinics.

B. Implanted NPs.

1. General: cochlear, phrenic nerve, deep brain and sacral stimulators

In the late 1950s and early 1960s, the first implantable cardiac pacemakers were developed⁴³. According to the National Institutes of Health, over 3 million cardiac pacemakers have since been implanted and the number may be in excess of 5 million. Cardiac pacemakers stimulate specialized cardiac muscle cells and so according to the above definition they are not NPs. However they are implanted stimulators that must remain functional in the hostile environment of the human body for many years. The development of the technology needed to achieve this led to a proliferation of a wide range of NPs in the late 1960s and early 1970s.

Individuals with diverse types of impairment and disability have benefited from the technology associated with the development of the cardiac pacemaker. Thousands of dorsal column

stimulators have since been implanted for pain control and spasticity⁴⁴. Dorsal column stimulators activate large sensory afferents in posterior spinal roots and in the dorsal columns. As mentioned above, according to the gate theory of pain, input from large afferents inhibits nociceptive transmission. Modified versions of dorsal column stimulators were later introduced for use as deep-brain stimulators (DBS)⁴⁵⁻⁴⁷. Several thousand patients have been implanted with DBS devices. DBS is often effective in counteracting tremor and bradykinesia in Parkinson's disease and reducing essential tremor by affecting the firing of neurons in the basal ganglia. Several competing theories have been proposed to explain these effects⁴⁸⁻⁵⁰. Phrenic nerve NPs that activate the diaphragm have also been implanted in their thousands (Fig. 2B^{51, 52}) as have vagus nerve stimulators for epilepsy (Fig. 2D). Radio-frequency-controlled NPs that stimulated the bladder detrusor muscle were implanted in a small number of individuals in the 1960s (Bradley *et al.*, 1963; Stenberg *et al.*, 1967). In 1997 the Medtronic Interstim sacral root stimulator (Fig. 2C) was approved by the FDA to treat urge incontinence and since then, according to Medtronic, 40,000 Interstim devices have been implanted. The Interstim has also been implanted off-label in a small number of SCI individuals in attempts to facilitate voiding (see below).

The most successful NP remains the cochlear stimulator (Clark *et al.*, 1977). Over 50,000 multichannel cochlear stimulators were implanted in the 1990s alone (Clark, 1999; Kessler, 1999). Cochlear stimulators and their associated external sound and speech processors and stimulus synthesizers are now at an advanced stage and provide a model for new generation NPs for motor control.

Advanced Concept Call-out

In spite of the growing numbers of implantable NPs and, in some cases, excellent clinical outcomes, some technical and physiological concerns remain. For example, difficulties and risks are involved in implanting multiple electrodes to activate widely distributed peripheral nerves. The long-term effects of chronic stimulation of populations of neurons in the brain, spinal cord or peripheral nerves remain to be fully explored.

2. Implanted devices for enhancing walking function

Progress in restoring limb movement with implantable NPs has been slow. The technical challenge of delivering trains of pulses to nerves innervating one or more muscle groups for several hours a day for many years is formidable. A small number of individuals were implanted with footdrop stimulators in pilot studies in the 1970s and 1980s⁵³⁻⁵⁵. The Waters and McNeal study⁵⁴ commenced in 1968 and led to the development by Medtronic Inc. (Minneapolis) of a sophisticated device called the *Neuromuscular Assist*® that included an underheel sensor that wirelessly triggered a portable external receiver/stimulator. This delivered power and stimulus commands through an external antenna taped to the skin to an implanted passive receiver. The receiver delivered pulse trains through a pair of electrodes in a silicone rubber flap wrapped around branches of the common peroneal nerve distal to the knee. Fifteen individuals were implanted. The system worked well in most of the recipients, in some cases for many years, but Medtronic decided not to pursue commercialization. Recently two models of implantable peroneal nerve stimulator have become available commercially in Europe, the Finetech STIMuSTEP® (www.finetech-medical.co.uk)⁵⁶ and the Neurodan ActiGait® (www.neurodan.com, Fig. 2A). In a phase II safety study 15 individuals with stroke with footdrop due to stroke were implanted with the ActiGait® system and showed improvements in gait⁵⁷. From a safety point of view, it was reported that the nerve cuffs in the device did not produce detectable reductions in nerve conduction velocity. Technical problems occurred, but were resolved at follow-ups⁵⁷. Like the Medtronic device, the STIMuSTEP® and

ActiGait® stimulators are triggered from an underheel sensor. A new innovation still at the experimental stage is the use of signals recorded in sensory nerves to trigger stimulation^{58, 59}.

FIG. 1 NEAR HERE

It should be noted that only a small minority of individuals with incomplete SCI benefit enough from the correction of footdrop alone to warrant the implantation of these devices. Multi-channel NPs that stimulate up to 16 muscles of the legs through percutaneous or fully implanted leads have been experimented with over the years⁶⁰⁻⁶³ but they are not commercially available. However, research in this area continues and recent results have been encouraging, particularly in relation to posture, standing and the avoidance of pressure ulcers (bedsores)⁶⁴⁻⁶⁸.

3. Intraspinal microstimulation

A radically different approach to NPs, namely intraspinal microstimulation (ISMS) has been explored in animal experiments in recent years⁶⁹. The method consists of implanting up to 16 microwires in the lumbosacral enlargement of the spinal cord (the region containing motoneurons innervating leg muscles). Stimulation through these microwires can activate single muscles or muscle synergies in normal animals⁷⁰. After some initial promise⁷¹, several implants in spinalized animals essentially revealed the technical limitations of the approach⁷². The implant surgeries took up to 12 hours. Manually positioning the electrodes in the right parts of the spinal cord to obtain the full set of desired synergies was difficult and rarely completely successful. After days or weeks the elicited movements changed, indicating migration of the microwires. In a trial in chronically implanted monkeys, co-contraction responses were often seen⁷³, which would make it hard or impossible to control movement in an NP application. The overall impression is that with current electrode technology ISMS is invasive, insufficiently reliable and therefore not ready for clinical application.

FIG. 2 NEAR HERE

4. Implanted devices for enhancing hand function

Regarding the upper extremity, after proof-of-principle trials with percutaneous leads, a fully implanted stimulator was developed at Case Western Reserve University (CWRU)⁷⁴. It was approved by the Food and Drug Administration in 1997 and marketed by Neurocontrol as the “Freehand System®” (Fig. 2E). About 200 of these systems were implanted in individuals with C4-C5 quadriplegia. Shoulder or wrist movements were used to control the stimulation of muscles in the forearm. An external control unit and antenna wirelessly activated an implanted receiver to generate pulse trains and stimulate the muscles selected by the external controller to produce different types of hand movement. Though all aspects of the technology and surgery were highly advanced and many recipients benefited significantly with improved hand function⁷⁵, the Freehand System® was ultimately withdrawn from the market in 2002. A fascinating analysis of the history of this and other NPs that showed clinical efficacy but did not survive commercially is to be found in a Princeton University thesis by Samuel W. Hall⁷⁶. Hall concludes “While the over-exuberant health care spending of the 1970s and early 1980s has taught policymakers a valuable lesson, the vicious cost-containment initiatives characteristic of current Medicare policy are outdated and have far-reaching negative effects on public health. The Centers for Medicare and Medicaid Services should replace their anti-technology bias with a payment system capable of recognizing the profound health economic benefits of neuroprostheses.”

An improved multi-channel version of the CWRU device has recently been implanted in seven individuals with SCI⁷⁷. The new device is controlled myoelectrically (i.e. via signals picked up from voluntarily activated muscles). It activates the biceps muscle as well as muscles controlling hand opening and grasp. Other recent research into novel implantable NPs for hand function include the Finetech STIMuGRIP®⁷⁸ and an implantable system called the Stimulus Router® that requires only the leads to be implanted, with pulse trains coupled through the skin from a wireless-triggered wristlet stimulator⁷⁹ (Fig. 3). The Stimulus Router is due to be tested in the first human recipients in mid-2008.

FIG. 3 NEAR HERE

5. Bladder Control

Bladder control is ranked the second most significant problem after loss of sex function among individuals with paraplegia and the fourth priority of individuals with quadriplegia⁸⁰. SCI can cause incontinence due to a loss of external urethral sphincter (EUS) contraction and/or an inability to void due to bladder-sphincter hyperactivity (dyssynergia). Untreated, this can lead to very high bladder pressures, vesico-ureteral reflux and eventual renal failure. It used to be the leading cause of death in people with SCI but dropped to fourth place after the widespread adoption of clean intermittent catheterization⁸¹.

Electrical stimulation for bladder control has been explored for over 40 years. Stimulation has been delivered variously to the inside of the bladder, bladder wall, thigh, pelvic floor, dorsal penile nerve, pelvic nerve, tibial nerve, sacral roots, sacral nerves and spinal cord. The successes and failures of these numerous approaches have recently been described in a detailed review⁸².

The first commercially available NP for bladder control derived from experiments in which voiding was elicited in spinalized animals by stimulation of sacral anterior roots⁸³⁻⁸⁵. Human trials of a sacral anterior root stimulator implant (SARSI) followed shortly thereafter⁸⁶. Brindley's device was commercialized as the Finetech-Brindley Bladder System® (Finetech Medical Ltd., Welwyn Garden City, UK). It has been implanted in over 2,500 people, in some cases for over 20 years⁸⁷. The main disadvantage of this device is that dorsal rhizotomies (cutting sensory nerves to the spinal cord) are required, resulting in an irreversible loss of sensory input from the genital organs. Another drawback is that anterior root stimulation activates the EUS as well as the bladder. Voiding is achieved in bursts by taking advantage of the slower relaxation time of the detrusor (bladder) muscle after short trains of stimuli. A recent study has shown that trapezoidal pulse waveforms can activate the bladder more selectively, thus improving the performance of SARSI implants⁸⁸.

Regarding incontinence, implanted sacral root stimulators (e.g. the Medtronic Interstim®) are currently the most successful implantable NPs for bladder control in a variety of neural disorders including SCI⁸⁹.

ISMS has been explored as an alternative means of eliciting voiding, but as in the case of locomotion, ISMS so far has not lived up to initial expectations. Pilot experiments in animals and humans in the 1970s showed that stimulation through pairs of relatively large intraspinal electrodes could elicit bladder contractions, but not without co-activating the EUS^{90,91}. More recent experiments have been performed with microwires implanted in the dorsal commissure of the spinal cord, which contains interneurons that inhibit EUS motoneurons⁹². Although reductions in

intraurethral pressure could be elicited in some implants, the more common outcome was activation^{82, 93}. It was subsequently shown that the dorsal commissure probably contains more interneurons that excite EUS motoneurons than those that inhibit them^{94, 95}. In a report published in October 2007, McCreery's group reported success in eliciting bladder contraction, concomitant EUS inhibition and voiding in two of three spinally transected cats by stimulating mainly within the dorsal columns⁹⁶. However, the voiding trials were performed during deep Propofol anesthesia. Urinary tract responses are suppressed by Propofol⁹⁷. Bladder and EUS responses to ISMS and pudendal nerve stimulation under deep anesthesia in spinal-cord-transected cats can change dramatically when the same animals are awake⁹⁸. Stimuli that relax the EUS under anesthesia are no longer as effective under normal awake conditions. Further evidence in awake SCI animals would be needed before clinical trials could be justified.

Other experimental approaches to bladder control with NPs include neuromodulation of sacral roots^{99, 100}; activation of reflexes evoked by selective stimulation of specific branches of the pudendal nerve¹⁰¹⁻¹⁰⁵ and high-frequency blockade of the pudendal nerve to inhibit the EUS¹⁰⁶⁻¹¹². It has recently been shown that activation and blockade of the pudendal nerve can be achieved with the stimulus router system in the awake SCI cat. This may provide a low-cost type of NP for either maintaining continence or eliciting voiding, as only two leads would be implanted^{111, 112}.

In recent years, over-optimistic forecasts of an imminent "cure" of SCI through neural regeneration and other restorative strategies have led many people with SCI to decline procedures that require dorsal rhizotomies. There is a growing realization that the cure is probably still a long way off, but the good news is that techniques such as pudendal nerve blockade and neuromodulation may soon provide alternative NP types that do not require rhizotomies.

IV. FACTORS INFLUENCING CHOICE

A. Level of injury

The level and completeness of SCI will determine the relevance of NPs to a particular individual. Phrenic nerve pacers are only relevant for high cervical injuries, typically at C3 and above. Upper extremity NPs are usually only effective for injuries in the range C4-C7. It is important to remember that NPs activate muscles via their nerves. Often motoneurons are destroyed at the epicenter of an injury. This is particularly troublesome at segmental level C7, because denervation can make it impossible to elicit hand opening and grasp. NPs for restoring locomotion can be useful in incomplete injuries at nearly all levels and also in complete injuries at low thoracic and lumbar levels where postural control is partially preserved. Likewise, bladder control NPs can be useful for nearly all levels of SCI, with the exception of cauda equina injuries, again because these are associated with denervation of the target muscles, in particular the EUS for bladder control.

B. Time after injury

There is little evidence-based consensus on the appropriate time after injury to commence the use of the various types of commercially available NPs. The same could of course be said of conventional physiotherapy. For example twenty years ago the accepted wisdom was that gait training should only start at an absolute minimum of 6 weeks after stroke, whereas today it starts as soon as it is

judged clinically to be safe, which can be within a few days in mild cases. Some NPs (e.g. surface muscle stimulators applied to the forearm or shoulder) can be used within a week or two of SCI to maintain muscle bulk and to ward off spasticity, contractures and shoulder subluxation (Fig. 1C). Others (e.g. SARI implants requiring rhizotomies) should only be considered after natural recovery has been allowed to run its full course (typically 1 year or more after injury).

C. Risks and contraindications

Certain side-effects or risks of electrical stimulation should always be taken into account when considering the use of NP devices.

FES in people with SCI at T6 level and above can trigger autonomic dysreflexia¹¹³. Originally this was attributed to nociceptive stimulation of the skin, but topical anesthesia did not change the response to FES, so it was concluded that muscle activation was the cause¹¹⁴. The larger the muscles stimulated, the greater the chance of triggering an episode of dysreflexia. Other side effects include pain or discomfort at high stimulus levels. There is a very wide range of tolerance between individuals in this regard. The cost-benefit ratio: although NP design is constantly improving, some devices still tend to be cumbersome and awkward to don and doff. The financial cost can be high, particularly in the case of implantable NPs. It is therefore important to have a clear idea of the functional gains that can reasonably be expected and to weigh these against cost and inconvenience.

Supramaximal stimulation of large leg muscles has caused patellar dislocation and even bone breakage in rare cases. Dried-out or faulty electrodes can cause skin burns, particularly in users with poor or lacking skin sensation. Implanted NPs carry a risk of post-implant infection. The risk is well established for cardiac pacemakers (~1%¹¹⁵) but not so well for NPs, which vary considerably in size and design. Generally, the larger the stimulator and the greater the number of leads, the greater the risk of infection. Lead breakages and migration tend to occur more in NPs than in cardiac pacemakers, necessitating relocation or explantation and replacement. Implanted microstimulators such as the Bion may also migrate, though it is too early to say how often this might happen.

V. SUMMARY.

In this chapter the historical origins of electrotherapy were briefly reviewed. The basic mechanism of electrical stimulation of nerves was described. Some of the key advances in the development of NPs were identified. The main types of NP used in the management of SCI were considered and the successes, limitations and failures of the NP approach were discussed. Finally, some of the factors influencing an SCI individual's choice of NP treatment were reviewed.

It is now recognized that when the use of NPs is combined with other treatments such as task-related exercise therapy, medications, Botox® and surgical procedures such as tendon transfers, significant improvements in function can result. In the near future, it is likely that NPs will increasingly be used in conjunction with devices that promote exercise training such as partial weight support robots and in-home telerehabilitation devices that allow remote supervision and game-playing to improve compliance¹¹⁶.

The treatment of incontinence has been one of the success stories of NPs. The control of bladder voiding in people with SCI remains a very important and elusive goal of NP research, but there have been some promising developments in this regard in the last 5 years.

The last decade has seen a big increase in the number of researchers around the world developing new NP devices and approaches. There has also been a significant increase in interest and investment on the part of government agencies and the medical electronics industry in this area. The next decade should see a significant increase in the range and availability of NPs, a lowering of their cost and an increase in the number and variety of clinical problems they can address.

VI. END OF CHAPTER QUESTIONS

Questions

1. How effective are NPs in the control of bladder function?
2. Can present-day NPs for the upper extremity provide clinically significant benefits, and if so, does this depend on the cervical level of the SCI?
3. NPs seem very hi-tech. Is it possible for therapists and clinicians who have little or no training in electronics, maths or physics to understand and use them?
4. What percentage of people with SCI find electrical stimulation uncomfortable or painful?
5. NPs are often very expensive, particularly implantables. What are the payment and reimbursement options?

Answers

1. Incontinence can be reduced in a significant proportion of SCI people with devices such as the Medtronic Interstim® sacral root stimulator. Percutaneous temporary implants are used to test whether a particular individual will benefit before a permanent implant is performed. Voiding is a more difficult problem, but recent research leaves room for optimism.
2. There are currently no commercially available surface stimulators for upper extremity that are convenient enough to be worn and used in daily life, though this will probably change within a year or two. The Bioness H200® is useful for therapeutic training in a clinical or static home setting. Combined with in-home telerehabilitation, significant functional gains can be anticipated. Regarding implantable NPs, the Freehand System® provided good outcomes for dozens of SCI recipients but it is no longer available. The STIMuGRIP® and Stimulus Router® systems may fill some of this gap, but they are still in the experimental stage. People with C5-7 injuries with preserved innervation of the muscles controlling hand opening and grasp benefit the most. Multi-channel systems for C4 complete SCI and incomplete injuries at even higher levels are still in the research phase.

3. The trend is to design NPs to be simple and easy to use for non-technically minded clinicians and end-users. As the numbers and variety of NPs increase, certain components will become more standardized (e.g. electrodes, user interfaces, computerized performance and compliance reports). The WalkAide® and Bioness H200® and L300® are among the new devices being widely used by therapists and clinicians without technical training.
4. In our experience, about 5% of people with good motor responses who could otherwise benefit from surface FES withdraw because of discomfort. A larger percentage eventually stop using their devices because of inconvenience. This will reduce as designs improve.
5. This varies tremendously between countries and across device types. CMS currently does not reimburse motor NPs, but it does reimburse muscles stimulators for back pain. This illogical situation may change as the benefits of NPs become more and more obvious and lobby groups and companies become more vocal. In Europe some countries such as the UK and Denmark already reimburse NPs. Implantables vary: dorsal column stimulators are reimbursed in most countries but upper extremity NPs are still considered experimental.

Acknowledgments

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Figure Legends

Fig. 1. Surface neuroprostheses. A. Medtronic Respond physiotherapy stimulator; B. Neuromove EMG-triggered stimulator; C. Stimulation of trapezius muscle to prevent shoulder subluxation; D. Ness Handmaster; E. University of Alberta Bionic Glove; F. Innovative Neurotronics WalkAide; G. Bioness L300.

Fig. 2. Implantable neuroprostheses. A. Neurodan B. Avery phrenic nerve pacer ; C. Medtronic Interstim sacral nerve stimulator ; D. Cyberonics vagal nerve stimulator; E. Neurocontrol Freehand system.

Fig. 3. Stimulus router system. A) cutaway view showing a surface electrode, implanted pick-up electrode, passive conductor and nerve cuff. B) cross-section showing current flowing between two surface electrodes, some being diverted through the implanted conductor to the nerve cuff and returning via forearm tissues. C. Schematic showing stimulator cuff containing surface electrodes that deliver current to hand opening and closing nerves via the implanted leads. The cuff is triggered from a wireless earpiece that detects small voluntary toothclicks.

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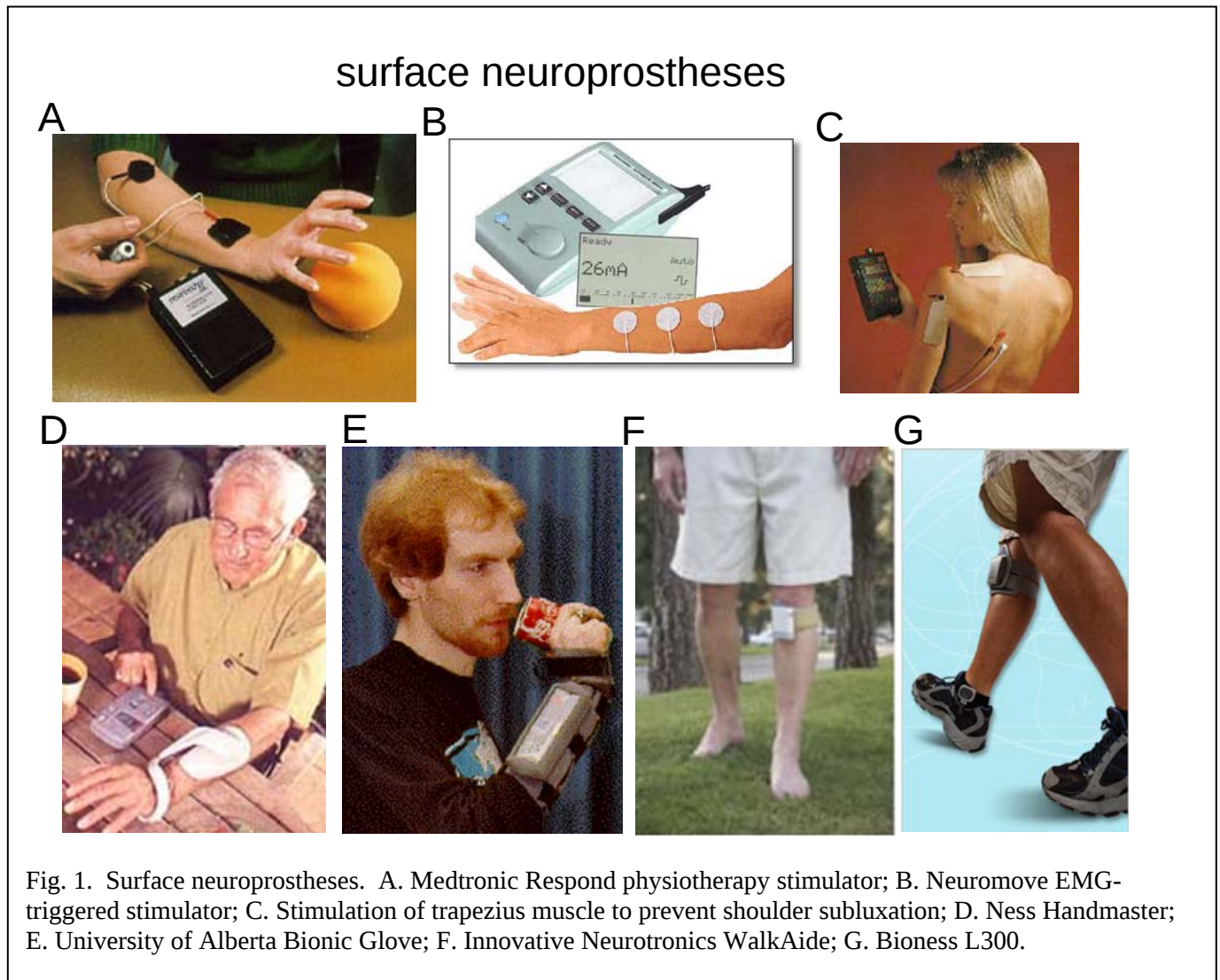
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Figures



implantable neuroprostheses

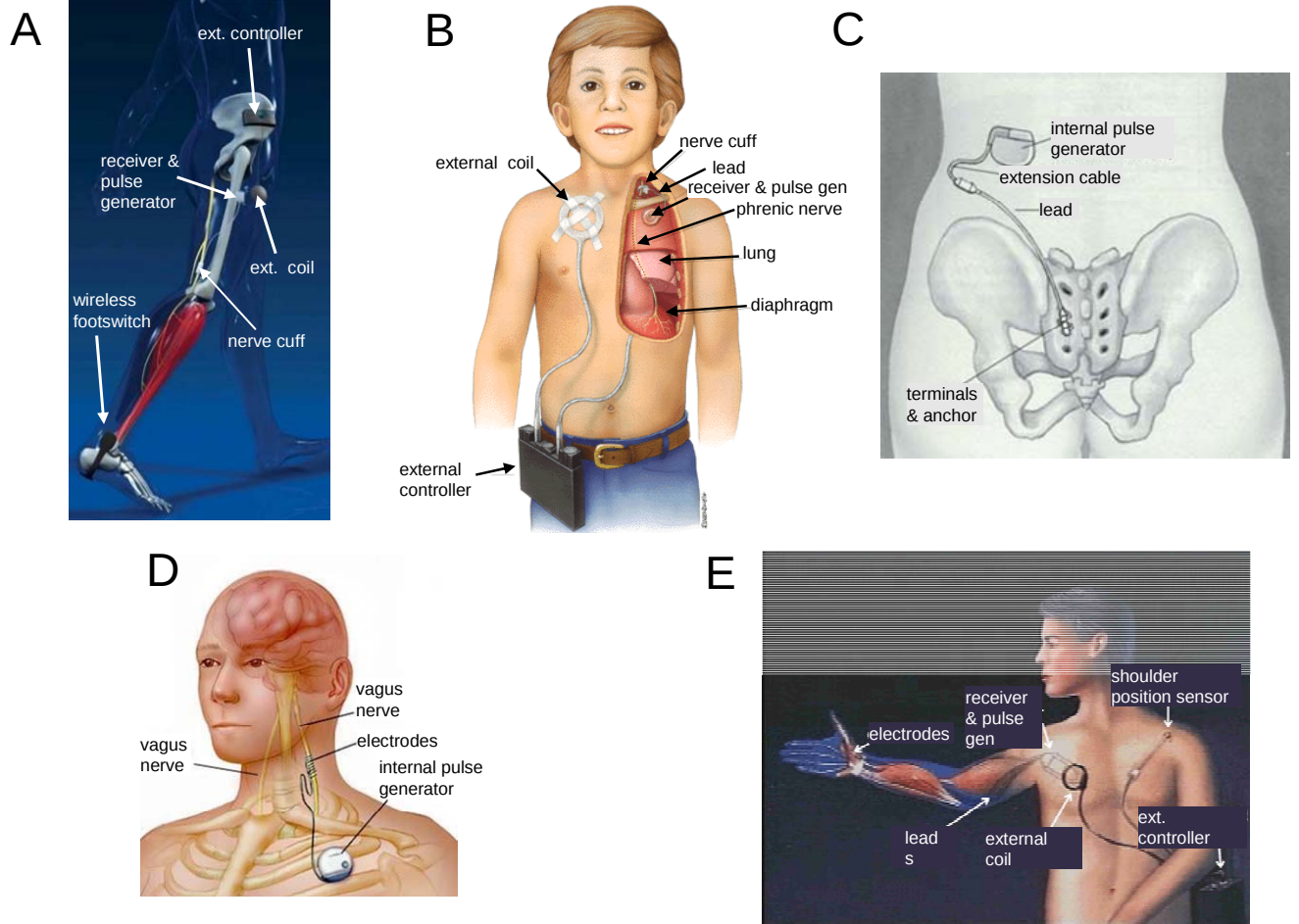


Fig. 2. Implantable Neuroprostheses. A. Neurodan B. Avery Phrenic Nerve Pacer ; C. Medtronic Interstim Sacral Nerve Stimulator ; D. Cyberonics Vagal Nerve Stimulator; E. Neurocontrol Freehand System.

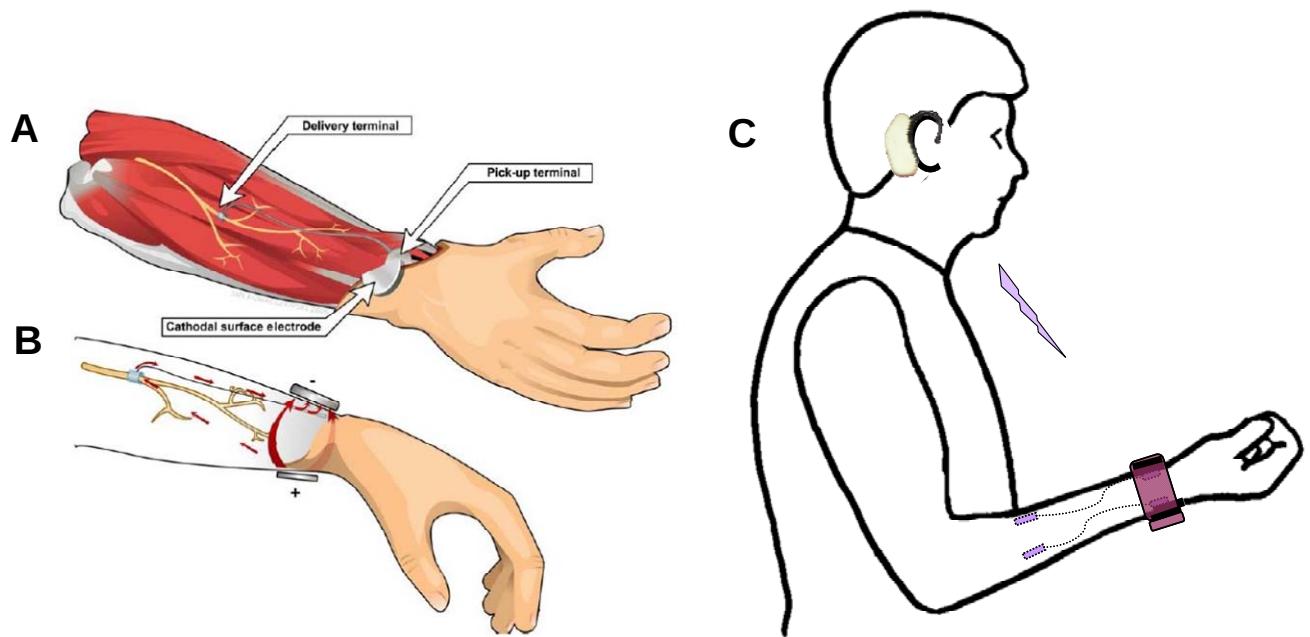


Fig. 3. Stimulus router system. A) cutaway view showing a surface electrode, implanted pick-up electrode, passive conductor and nerve cuff. B) cross-section showing current flowing between two surface electrodes, some being diverted through the implanted conductor to the nerve cuff and returning via forearm tissues. C. Schematic showing stimulator cuff containing surface electrodes that deliver current to hand opening and closing nerves via the implanted leads. The cuff is triggered from a wireless earpiece that detects small voluntary toothclicks.